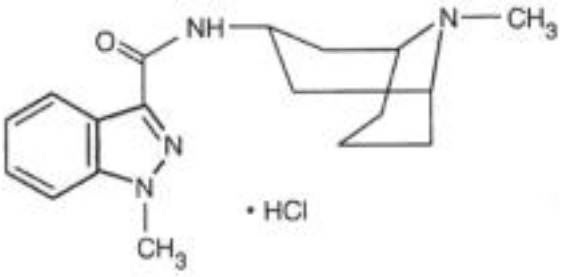
GRANISETRON HYDROCHLORIDE - granisetron hydrochloride injection
Akorn Inc.

Rx only

DESCRIPTION

Granisetron Hydrochloride Injection (granisetron hydrochloride) is an antinauseant and antiemetic agent. Chemically it is *endo*-N-(9-methyl-9-azabicyclo [3.3.1] non-3-yl)-1-methyl-1H-indazole-3-carboxamide hydrochloride with a molecular weight of 348.9 (312.4 free base). Its empirical formula is $C_{18}H_{24}N_4O$•HCl, while its chemical structure is:



granisetron hydrochloride

Granisetron hydrochloride is a white to off-white solid that is readily soluble in water and normal saline at 20°C. Granisetron Injection is a clear, colorless, sterile, nonpyrogenic, aqueous solution for intravenous administration.
Granisetron Hydrochloride Injection 1 mg/mL is available in 1 mL Single-Use and 4 mL Multi-Use vials. Granisetron Hydrochloride Injection 0.1 mg/mL is available in a 1 mL Single-Use vial.
1 mg/mL: Each mL contains:
Active: Granisetron hydrochloride 1.12 mg, equivalent to granisetron, 1 mg;
Preservative: Benzyl Alcohol, 10 mg;
Inactives: Sodium Chloride, 9 mg; Citric Acid, 2 mg; Sodium Citrate, Dihydrate, Sodium Hydroxide and/or Hydrochloric Acid may be added to adjust pH (approximately 4.0 to 6.0), and Water for Injection q.s. to 1 mL.
0.1 mg/mL: Each mL contains:
Active: Granisetron hydrochloride 0.112 mg, equivalent to granisetron, 0.1 mg;
Preservative: None;
Inactives: Sodium Chloride, 9 mg; Citric Acid, 2 mg; Sodium Citrate, Dihydrate, Sodium Hydroxide and/or Hydrochloric Acid may be added to adjust pH (approximately 4.0 to 6.0), and Water for Injection q.s. to 1 mL.

CLINICAL PHARMACOLOGY

Granisetron is a selective 5-hydroxytryptamine$_3$ (5-HT$_3$) receptor antagonist with little or no affinity for other serotonin receptors, including 5-HT$_1$; 5-HT$_{1A}$; 5-HT$_{1B/C}$; 5-HT$_2$; for alpha$_1$-, alpha$_2$- or beta-adrenoreceptors; for dopamine-D$_2$; or for histamine-H$_1$; benzodiazepine; picrotoxin or opioid receptors.
Serotonin receptors of the 5-HT$_3$ type are located peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postrema. During chemotherapy-induced vomiting, mucosal enterochromaffin cells release serotonin, which stimulates 5-HT$_3$ receptors. This evokes vagal afferent discharge and may induce vomiting. Animal studies demonstrate that, in binding to 5-HT$_3$ receptors, granisetron blocks serotonin stimulation and subsequent vomiting after emetogenic stimuli such as cisplatin. In the ferret animal model, a single granisetron injection prevented vomiting due to high-dose cisplatin or arrested vomiting within 5 to 30 seconds.
In most human studies, granisetron has had little effect on blood pressure, heart rate or ECG. No evidence of an effect on plasma prolactin or aldosterone concentrations has been found in other studies.
Granisetron Injection exhibited no effect on oro-cecal transit time in normal volunteers given a single intravenous infusion of 50 mcg/kg or 200 mcg/kg. Single and multiple oral doses slowed colonic transit in normal volunteers.

Pharmacokinetics

Chemotherapy-Induced Nausea and Vomiting
In adult cancer patients undergoing chemotherapy and in volunteers, mean pharmacokinetic data obtained from an infusion of a single 40 mcg/kg dose of Granisetron Injection are shown in **Table 1**.

Table 1. Pharmacokinetic Parameters in Adult Cancer Patients Undergoing Chemotherapy and in Volunteers, Following a Single Intravenous 40 mcg/kg Dose of Granisetron Injection

	Peak Plasma	Terminal Phase	Total	Volume of

	Concentration (ng/mL)	Plasma Half-Life (h)	Clearance (L/h/kg)	Distribution (L/kg)
Cancer Patients				
Mean	63.8*	8.95*	0.38*	3.07*
Range	18.0 to 176	0.90 to 31.1	0.14 to 1.54	0.85 to 10.4
Volunteers				
21 to 42 years				
Mean	64.3†	4.91†	0.79†	3.04†
Range	11.2 to 182	0.88 to 15.2	0.20 to 2.56	1.68 to 6.13
65 to 81 years				
Mean	57.0†	7.69†	0.44†	3.97†
Range	14.6 to 153	2.65 to 17.7	0.17 to 1.06	1.75 to 7.01

*5-minute infusion.

†3-minute infusion.

Distribution
Plasma protein binding is approximately 65% and granisetron distributes freely between plasma and red blood cells.

Metabolism
Granisetron metabolism involves N-demethylation and aromatic ring oxidation followed by conjugation. *In vitro* liver microsomal studies show that granisetron's major route of metabolism is inhibited by ketoconazole, suggestive of metabolism mediated by the cytochrome P-450 3A subfamily. Animal studies suggest that some of the metabolites may also have 5-HT_3 receptor antagonist activity.

Elimination
Clearance is predominantly by hepatic metabolism. In normal volunteers, approximately 12% of the administered dose is eliminated unchanged in the urine in 48 hours. The remainder of the dose is excreted as metabolites, 49% in the urine, and 34% in the feces.

Subpopulations

Gender
There was high inter- and intra-subject variability noted in these studies. No difference in mean AUC was found between males and females, although males had a higher C_{max} generally.

Elderly
The ranges of the pharmacokinetic parameters in elderly volunteers (mean age 71 years), given a single 40 mcg/kg intravenous dose of Granisetron Injection, were generally similar to those in younger healthy volunteers; mean values were lower for clearance and longer for half-life in the elderly patients (see **Table 1**).

Pediatric Patients
A pharmacokinetic study in pediatric cancer patients (2 to 16 years of age), given a single 40 mcg/kg intravenous dose of Granisetron Injection, showed that volume of distribution and total clearance increased with age. No relationship with age was observed for peak plasma concentration or terminal phase plasma half-life. When volume of distribution and total clearance are adjusted for body weight, the pharmacokinetics of granisetron are similar in pediatric and adult cancer patients.

Renal Failure Patients
Total clearance of granisetron was not affected in patients with severe renal failure who received a single 40 mcg/kg intravenous dose of Granisetron Injection.

Hepatically Impaired Patients
A pharmacokinetic study in patients with hepatic impairment due to neoplastic liver involvement showed that total clearance was approximately halved compared to patients without hepatic impairment. Given the wide variability in pharmacokinetic parameters noted in patients and the good tolerance of doses well above the recommended 10 mcg/kg dose, dosage adjustment in patients with possible hepatic functional impairment is not necessary.

CLINICAL TRIALS

Chemotherapy-Induced Nausea and Vomiting

Single-Day Chemotherapy

Cisplatin-Based Chemotherapy
In a double-blind, placebo-controlled study in 28 cancer patients, Granisetron Injection, administered as a single intravenous infusion of 40 mcg/kg, was significantly more effective than placebo in preventing nausea and vomiting induced by cisplatin chemotherapy (see **Table 2**).

Table 2. Prevention of Chemotherapy-Induced Nausea and Vomiting—Single-Day Cisplatin Therapy*

	Granisetron Injection	Placebo	P-Value
Number of Patients	14	14	
Response Over 24 Hours			
Complete Response†	93%	7%	<0.001
No Vomiting	93%	14%	<0.001
No More Than Mild Nausea	93%	7%	<0.001

* Cisplatin administration began within 10 minutes of Granisetron Injection infusion and continued for 1.5 to 3.0 hours. Mean cisplatin dose was 86 mg/m^2 in the Granisetron Injection group and 80 mg/m^2 in the placebo group.

† No vomiting and no moderate or severe nausea.

Granisetron Injection was also evaluated in a randomized dose response study of cancer patients receiving cisplatin ≥75 mg/m^2. Additional chemotherapeutic agents included: anthracyclines, carboplatin, cytostatic antibiotics, folic acid derivatives, methylhydrazine, nitrogen mustard analogs, podophyllotoxin derivatives, pyrimidine analogs, and vinca alkaloids. Granisetron Injection doses of 10 and 40 mcg/kg were superior to 2 mcg/kg in preventing cisplatin-induced nausea and vomiting, but 40 mcg/kg was not significantly superior to 10 mcg/kg (see **Table 3**).

Table 3. Prevention of Chemotherapy-Induced Nausea and Vomiting—Single-Day High-Dose Cisplatin Therapy*

	Granisetron Injection (mcg/kg)			P-Value (vs. 2 mcg/kg)	
	2	10	40	10	40
Number of Patients	52	52	53		
Response Over 24 Hours					
Complete Response†	31%	62%	68%	<0.002	<0.001 <0.001
No Vomiting	38%	65%	74%	<0.001	0.007
No More Than Mild Nausea	58%	75%	79%	NS	

* Cisplatin administration began within 10 minutes of Granisetron Injection infusion and continued for 2.6 hours (mean). Mean cisplatin doses were 96 to 99 mg/m^2.

† No vomiting and no moderate or severe nausea.

Granisetron Injection was also evaluated in a double-blind, randomized dose response study of 353 patients stratified for high (≥80 to 120 mg/m^2) or low (50 to 79 mg/m^2) cisplatin dose. Response rates of patients for both cisplatin strata are given in **Table 4**.

Table 4. Prevention of Chemotherapy-Induced Nausea and Vomiting—Single-Day High-Dose and Low-Dose Cisplatin Therapy*

	Granisetron Injection (mcg/kg)				P-Value (vs. 5 mcg/kg)		
	5	10	20	40	10	20	40
High-Dose Cisplatin Number of Patients	40	49	48	47			
Response Over 24 Hours							
Complete Response†	18%	41%	40%	47%	0.018	0.025	0.004
No Vomiting	28%	47%	44%	53%	NS	NS	0.016

No Nausea	15%	35%	38%	43%	0.036	0.019	0.005
Low-Dose Cisplatin	42	41	40	46			
Number of Patients							
Response Over 24 Hours							
Complete Response†	29%	56%	58%	41%	0.012	0.009	NS
No Vomiting	36%	63%	65%	43%	0.012	0.008	NS
No Nausea	29%	56%	38%	33%	0.012	NS	NS

* Cisplatin administration began within 10 minutes of Granisetron Injection infusion and continued for 2 hours (mean). Mean cisplatin doses were 64 and 98 mg/m^2 for low and high strata.

† No vomiting and no use of rescue antiemetic.

For both the low and high cisplatin strata, the 10, 20, and 40 mcg/kg doses were more effective than the 5 mcg/kg dose in preventing nausea and vomiting within 24 hours of chemotherapy administration. The 10 mcg/kg dose was at least as effective as the higher doses.

Moderately Emetogenic Chemotherapy

Granisetron Injection, 40 mcg/kg, was compared with the combination of chlorpromazine (50 to 200 mg/24 hours) and dexamethasone (12 mg) in patients treated with moderately emetogenic chemotherapy, including primarily carboplatin >300 mg/m^2, cisplatin 20 to 50 mg/m^2 and cyclophosphamide >600 mg/m^2. Granisetron Injection was superior to the chlorpromazine regimen in preventing nausea and vomiting (see **Table 5**).

Table 5. Prevention of Chemotherapy-Induced Nausea and Vomiting—Single-Day Moderately Emetogenic Chemotherapy

	Granisetron Injection	**Chlorpromazine***	**P-Value**
Number of Patients	133	133	
Response Over 24 Hours			
Complete Response†	68%	47%	<0.001
No Vomiting	73%	53%	<0.001
No More Than Mild Nausea	77%	59%	<0.001

* Patients also received dexamethasone, 12 mg.

† No vomiting and no moderate or severe nausea.

In other studies of moderately emetogenic chemotherapy, no significant difference in efficacy was found between Granisetron doses of 40 mcg/kg and 160 mcg/kg.

Repeat-Cycle Chemotherapy

In an uncontrolled trial, 512 cancer patients received Granisetron Injection, 40 mcg/kg, prophylactically, for two cycles of chemotherapy, 224 patients received it for at least four cycles, and 108 patients received it for at least six cycles. Granisetron Injection efficacy remained relatively constant over the first six repeat cycles, with complete response rates (no vomiting and no moderate or severe nausea in 24 hours) of 60% to 69%. No patients were studied for more than 15 cycles.

Pediatric Studies

A randomized double-blind study evaluated the 24-hour response of 80 pediatric cancer patients (age 2 to 16 years) to Granisetron Injection 10, 20 or 40 mcg/kg. Patients were treated with cisplatin ≥60 mg/m^2, cytarabine ≥3 g/m^2, cyclophosphamide ≥1 g/m^2 or nitrogen mustard ≥6 mg/m^2 (see **Table 6**).

Table 6. Prevention of Chemotherapy-Induced Nausea and Vomiting in Pediatric Patients

	Granisetron Injection Dose (mcg/kg)		
	10	**20**	**40**
Number of Patients	29	26	25
Median Number of Vomiting Episodes	2	3	1
Complete Response Over 24 Hours*	21%	31%	32%

* No vomiting and no moderate or severe nausea.

A second pediatric study compared Granisetron Injection 20 mcg/kg to chlorpromazine plus dexamethasone in 88 patients treated with ifosfamide ≥3 g/m^2/day for two or three days. Granisetron Injection was administered on each day of ifosfamide treatment. At 24 hours, 22% of Granisetron Injection patients achieved complete response (no vomiting and no moderate or severe nausea in 24 hours) compared with 10% on the chlorpromazine regimen. The median number of vomiting episodes with Granisetron Injection was 1.5; with chlorpromazine it was 7.0.

INDICATIONS AND USAGE

Granisetron Injection is indicated for:

- The prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.

CONTRAINDICATIONS

Granisetron Injection is contraindicated in patients with known hypersensitivity to the drug or to any of its components.

WARNINGS

Hypersensitivity reactions may occur in patients who have exhibited hypersensitivity to other selective 5-HT_3 receptor antagonists.

PRECAUTIONS

Granisetron is not a drug that stimulates gastric or intestinal peristalsis. It should not be used instead of nasogastric suction. The use of Granisetron in patients with chemotherapy-induced nausea and vomiting may mask a progressive ileus and/or gastric distention.

Drug Interactions

Granisetron does not induce or inhibit the cytochrome P-450 drug-metabolizing enzyme system *in vitro*. There have been no definitive drug-drug interaction studies to examine pharmacokinetic or pharmacodynamic interaction with other drugs; however, in humans, Granisetron Injection has been safely administered with drugs representing benzodiazepines, neuroleptics and anti-ulcer medications commonly prescribed with antiemetic treatments. Granisetron Injection also does not appear to interact with emetogenic cancer chemotherapies. Because granisetron is metabolized by hepatic cytochrome P-450 drug-metabolizing enzymes, inducers, or inhibitors of these enzymes may change the clearance and, hence, the half-life of granisetron. No specific interaction studies have been conducted in anesthetized patients. In addition, the activity of the cytochrome P-450 subfamily 3A4 (involved in the metabolism of some of the main narcotic analgesic agents) is not modified by Granisetron *in vitro*.

In *in vitro* human microsomal studies, ketoconazole inhibited ring oxidation of Granisetron. However, the clinical significance of *in vivo* pharmacokinetic interactions with ketoconazole is not known. In a human pharmacokinetic study, hepatic enzyme induction with phenobarbital resulted in a 25% increase in total plasma clearance of intravenous Granisetron. The clinical significance of this change is not known.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 24-month carcinogenicity study, rats were treated orally with granisetron 1, 5 or 50 mg/kg/day (6, 30 or 300 mg/m^2/day). The 50 mg/kg/day dose was reduced to 25 mg/kg/day (150 mg/m^2/day) during week 59 due to toxicity. For a 50 kg person of average height (1.46 m^2 body surface area), these doses represent 16, 81 and 405 times the recommended clinical dose (0.37 mg/m^2, iv) on a body surface area basis. There was a statistically significant increase in the incidence of hepatocellular carcinomas and adenomas in males treated with 5 mg/kg/day (30 mg/m^2/day, 81 times the recommended human dose based on body surface area) and above, and in females treated with 25 mg/kg/day (150 mg/m^2/day, 405 times the recommended human dose based on body surface area). No increase in liver tumors was observed at a dose of 1 mg/kg/day (6 mg/m^2/day, 16 times the recommended human dose based on body surface area) in males and 5 mg/kg/day (30 mg/m^2/day, 81 times the recommended human dose based on body surface area) in females. In a 12-month oral toxicity study, treatment with granisetron 100 mg/kg/day (600 mg/m^2/day, 1622 times the recommended human dose based on body surface area) produced hepatocellular adenomas in male and female rats while no such tumors were found in the control rats. A 24-month mouse carcinogenicity study of granisetron did not show a statistically significant increase in tumor incidence, but the study was not conclusive.

Because of the tumor findings in rat studies, Granisetron Injection should be prescribed only at the dose and for the indication recommended (see **INDICATIONS AND USAGE** and **DOSAGE AND ADMINISTRATION**).

Granisetron was not mutagenic in an *in vitro* Ames test and mouse lymphoma cell forward mutation assay, and *in vivo* mouse micronucleus test and *in vitro* and *ex vivo* rat hepatocyte UDS assays. It, however, produced a significant increase in UDS in HeLa cells *in vitro* and a significant increased incidence of cells with polyploidy in an *in vitro* human lymphocyte chromosomal aberration test.

Granisetron at subcutaneous doses up to 6 mg/kg/day (36 mg/m^2/day, 97 times the recommended human dose based on body surface area) was found to have no effect on fertility and reproductive performance of male and female rats.

Pregnancy

Teratogenic Effects-Pregnancy Category B

Reproduction studies have been performed in pregnant rats at intravenous doses up to 9 mg/kg/day (54 mg/m^2/day, 146 times the recommended human dose based on body surface area) and pregnant rabbits at intravenous doses up to 3 mg/kg/day (35.4 mg/m^2/day, 96 times the recommended human dose based on body surface area) and have revealed no evidence of impaired fertility or harm to the fetus due to granisetron. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Benzyl alcohol may cross the placenta. Granisetron Injection 1 mg/mL is preserved with benzyl alcohol and should be used in pregnancy only if the benefit outweighs the potential risk.

Nursing Mothers

It is not known whether granisetron is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Granisetron Injection is administered to a nursing woman.

Pediatric Use

See **DOSAGE AND ADMINISTRATION** for use in chemotherapy-induced nausea and vomiting in pediatric patients 2 to 16 years of age. Safety and effectiveness in pediatric patients under 2 years of age have not been established.

Benzyl alcohol, a component of Granisetron 1 mg/mL, has been associated with serious adverse events and death, particularly in neonates. The “gasping syndrome,” characterized by central nervous system depression, metabolic acidosis, gasping respirations, and high levels of benzyl alcohol and metabolites in blood and urine, has been associated with benzyl alcohol dosages >99 mg/kg/day in neonates and low birth weight neonates. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. Although normal therapeutic doses of this product deliver amounts of benzyl alcohol that are substantially lower than those reported in association with the “gasping syndrome,” the minimum amount of benzyl alcohol at which toxicity may occur is not known. Premature and low birth-weight infants, as well as patients receiving high dosages, may be more likely to develop toxicity. Practitioners administering this and other medications containing benzyl alcohol should consider the combined daily metabolic load of benzyl alcohol from all sources.

Geriatric Use

During chemotherapy clinical trials, 713 patients 65 years of age or older received Granisetron Injection. Effectiveness and safety were similar in patients of various ages.

ADVERSE REACTIONS

Chemotherapy-Induced Nausea and Vomiting

The following have been reported during controlled clinical trials or in the routine management of patients. The percentage figures are based on clinical trial experience only. **Table 7** gives the comparative frequencies of the five most commonly reported adverse events (≥3%) in patients receiving Granisetron Injection, in single-day chemotherapy trials. These patients received chemotherapy, primarily cisplatin, and intravenous fluids during the 24-hour period following Granisetron Injection administration. Events were generally recorded over seven days post-Granisetron Injection administration. In the absence of a placebo group, there is uncertainty as to how many of these events should be attributed to Granisetron, except for headache, which was clearly more frequent than in comparison groups.

Table 7. Principal Adverse Events in Clinical Trials — Single-Day Chemotherapy

	Percent of Patients With Event	
	Granisetron Injection 40 mcg/kg (n=1268)	**Comparator* (n=422)**
Headache	14%	6%
Asthenia	5%	6%
Somnolence	4%	15%
Diarrhea	4%	6%
Constipation	3%	3%

* Metoclopramide/dexamethasone and phenothiazines/dexamethasone.

In over 3,000 patients receiving Granisetron Injection (2 to 160 mcg/kg) in single-day and multiple-day clinical trials with emetogenic cancer therapies, adverse events, other than those in **Table 7**, were observed; attribution of many of these events to Granisetron is uncertain.

Hepatic
In comparative trials, mainly with cisplatin regimens, elevations of AST and ALT (>2 times the upper limit of normal) following administration of Granisetron Injection occurred in 2.8% and 3.3% of patients, respectively. These frequencies were not significantly different from those seen with comparators (AST: 2.1%; ALT: 2.4%).

Cardiovascular
Hypertension (2%); hypotension, arrhythmias such as sinus bradycardia, atrial fibrillation, varying degrees of A-V block, ventricular ectopy including non-sustained tachycardia, and ECG abnormalities have been observed rarely.

Central Nervous System
Agitation, anxiety, CNS stimulation and insomnia were seen in less than 2% of patients. Extrapyramidal syndrome occurred rarely and only in the presence of other drugs associated with this syndrome.

Hypersensitivity
Rare cases of hypersensitivity reactions, sometimes severe (eg, anaphylaxis, shortness of breath, hypotension, urticaria) have been reported.

Other
Fever (3%), taste disorder (2%), skin rashes (1%). In multiple-day comparative studies, fever occurred more frequently with Granisetron Injection (8.6%) than with comparative drugs (3.4%, $P<0.014$), which usually included dexamethasone.

OVERDOSAGE
There is no specific antidote for Granisetron Injection overdosage. In case of overdosage, symptomatic treatment should be given. Overdosage of up to 38.5 mg of granisetron hydrochloride injection has been reported without symptoms or only the occurrence of a slight headache.

DOSAGE AND ADMINISTRATION
NOTE: GRANISETRON 1 MG/ML CONTAINS BENZYL ALCOHOL (see **PRECAUTIONS**).

Prevention of Chemotherapy-Induced Nausea and Vomiting
The recommended dosage for Granisetron Injection is 10 mcg/kg administered intravenously within 30 minutes before initiation of chemotherapy, and only on the day(s) chemotherapy is given.

Infusion Preparation
Granisetron Injection may be administered intravenously either undiluted over 30 seconds, or diluted with 0.9% Sodium Chloride or 5% Dextrose and infused over 5 minutes.

Stability
Intravenous infusion of Granisetron Injection should be prepared at the time of administration. However, Granisetron Injection has been shown to be stable for at least 24 hours when diluted in 0.9% Sodium Chloride or 5% Dextrose and stored at room temperature under normal lighting conditions.

As a general precaution, Granisetron Injection should not be mixed in solution with other drugs. Parenteral drug products should be inspected visually for particulate matter and discoloration before administration whenever solution and container permit.

Pediatric Patients
The recommended dose in pediatric patients 2 to 16 years of age is 10 mcg/kg (see **CLINICAL TRIALS**). Pediatric patients under 2 years of age have not been studied.

Geriatric Patients, Renal Failure Patients or Hepatically Impaired Patients
No dosage adjustment is recommended (see **CLINICAL PHARMACOLOGY: Pharmacokinetics**).

HOW SUPPLIED
Granisetron Injection, 1 mg/mL (free base), is supplied in 1 mL Single-Use Vials and 4 mL Multi-Use Vials. CONTAINS BENZYL ALCOHOL.

NDC 17478-546-01 (package of 10 Single-Use Vials)

NDC 17478-546-04 (package of 10 Multi-Use Vials)

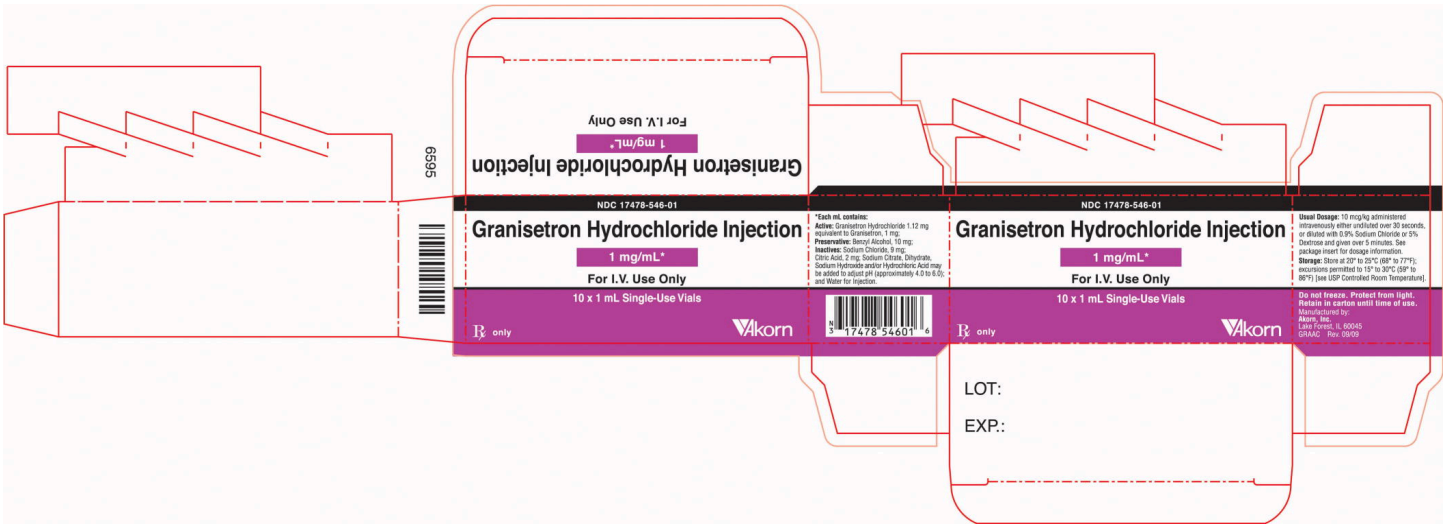
Granisetron Injection, 0.1 mg/mL (free base), is supplied in 1 mL Single-Use Vials. CONTAINS NO PRESERVATIVE.

NDC 17478-547-01 (package of 10 Single-Use Vials)

Storage
Store single-use vials and multi-use vials at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].
Once the multi-use vial is penetrated, its contents should be used within 30 days. Do not freeze. Protect from light.
Manufactured by:
Akorn, Inc.
Lake Forest, IL 60045
GR00N
Rev. 09/09

GRANISETRON HYDROCHLORIDE INJECTION CONTAINER LABEL PRINCIPAL DISPLAY PANEL TEXT:
NDC 17478-546-01
Granisetron
Hydrochloride
Injection
1 mg/mL
For I.V. Use Only
1 mL Single-Use Vial
Store at 20° to 25°C (68°
to 77°F). Do Not Freeze.
Protect From Light.
Rx only
GRAAL Mfg. by:
Rev. 09/09 Akorn, Inc.
LOT
EXP.

GRANISETRON HYDROCHLORIDE INJECTION CARTON LABEL PRINCIPAL DISPLAY PANEL TEXT:
NDC 17478-546-01
Granisetron Hydrochloride Injection
1 mg/mL*
For I.V. Use Only
10 x 1 mL Single-Use Vials
Rx only Akorn



GRANISETRON HYDROCHLORIDE INJECTION CONTAINER LABEL PRINCIPAL DISPLAY PANEL TEXT:

NDC 17478-546-04
Granisetron Hydrochloride Injection
4 mg/4 mL
(1 mg/mL)
For I.V. Use Only
Multi-Use Vial
Store at 20° to 25°C
(68° to 77°F).
Do Not Freeze.
Protect From Light.
Rx only
GRABL Mfg. by:
Rev. 09/09 Akorn, Inc.
LOT
EXP.

GRANISETRON HYDROCHLORIDE INJECTION CARTON LABEL PRINCIPAL DISPLAY PANEL TEXT:

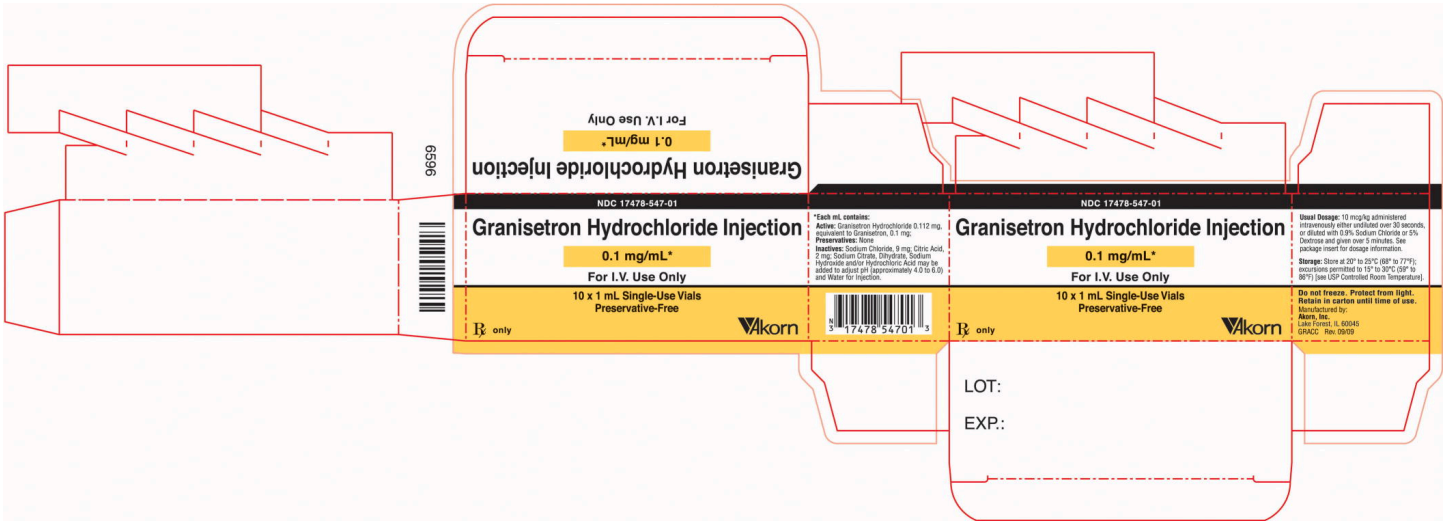
NDC 17478-546-04
Granisetron Hydrochloride Injection
4 mg/4 mL (1 mg/mL)*
For I.V. Use Only
10 x 4 mL Multi-Use Vials
Rx only Akorn

GRANISETRON HYDROCHLORIDE INJECTION CONTAINER LABEL PRINCIPAL DISPLAY PANEL TEXT:

NDC 17478-547-01
Granisetron Hydrochloride Injection
0.1 mg/mL
For I.V. Use Only
1 mL Single-Use Vial
Store at 20° to 25°C (68°
to 77°F). Do Not Freeze.
Protect From Light.
Rx only
GRACL Mfg. by:
Rev. 09/09 Akorn, Inc.
LOT
EXP.

GRANISETRON HYDROCHLORIDE INJECTION CARTON LABEL PRINCIPAL DISPLAY PANEL TEXT:

NDC 17478-547-01
Granisetron Hydrochloride Injection
0.1 mg/mL*
For I.V. Use Only
10 x 1 mL Single-Use Vials
Preservative-Free
Rx only Akorn


6596
Granisetron Hydrochloride Injection
0.1 mg/mL*
For I.V. Use Only
NDC 17478-547-01
Granisetron Hydrochloride Injection
0.1 mg/mL*
For I.V. Use Only
10 x 1 mL Single-Use Vials
Preservative-Free
℞ only
Akorn
*Each mL contains:
Active: Granisetron Hydrochloride 0.112 mg, equivalent to Granisetron, 0.1 mg.
Preservatives: None
Inactives: Sodium Chloride, 9 mg; Citric Acid, 2 mg; Sodium Citrate, Dihydrate, Sodium Hydroxide and/or Hydrochloric Acid may be added to adjust pH (approximately 4.0 to 6.0) and Water for Injection.
3 17478 54701 3
NDC 17478-547-01
Granisetron Hydrochloride Injection
0.1 mg/mL*
For I.V. Use Only
10 x 1 mL Single-Use Vials
Preservative-Free
℞ only
Akorn
Usual Dosage: 10 mcg/kg administered intravenously either undiluted over 30 seconds, or diluted with 0.9% Sodium Chloride or 5% Dextrose and given over 5 minutes. See package insert for dosage information.
Storage: Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].
Do not freeze. Protect from light. Retain in carton until time of use.
Manufactured by:
Akorn, Inc.
Lake Forest, IL 60045
GRACO: Rev. 09/09
LOT:
EXP.: